was: Na^+ 110 mmol/litre, K^+ 3.3 mmol/litre, urea 1.9 mmol/litre, and creatinine 64 mmol/litre. Her urine sodium and osmolarity were not determined.

She had been off all neuroleptics for six months, but had been prescribed lofepramine (140 mg daily) four weeks before her presentation. The hyponatraemia persisted until her lofepramine was stopped, and within 36 hours it resolved. It is of interest that she had been on fluphenazine, haloperidol, trifluoperazine, iprindole, and amitriptyline in the past without any undue effect.

It is likely that her condition was precipitated by lofepramine. However, we were unable to confirm this conclusively, since it would have needed a challenge test to do so. However, we hope that this case will draw attention to the possibility of a drug-induced hyponatraemia in psychiatric patients.

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Clomipramine and Flupenthixol – Additive Antidepressants?

SIR: The possibility that flupenthixol and tricyclics would have an additive antidepressant effect was first suggested by Reiter (1969), although the combination has never been specifically evaluated. This report shows the effect of manipulating flupenthixol dose when a stable tricyclic regime is being given concurrently.

Case report: A 31-year-old female with a severe, recurrent, unipolar, depressive psychosis met RDC criteria (Spitzer *et al*, 1977) for major depressive disorder, endogenous, psychotic, and retarded sub-types. She was non-delusional, but had suicidal and homicidal hallucinations. She was a DST non-suppressor, and had a Hamilton score of 38. In the first 25 months of her third episode, she was refractory to treatment with tricyclic antidepressants, lithium/tricyclic, tricyclic/antipsychotic, and lithium/tricyclic/antipsychotic combinations, carbamazepine and ECT. Marital therapy, cognitive-behaviour therapy, light-exposure and an exclusion diet were similarly ineffective.

At that time, her medication was changed to clomipramine (300 mg/day), L-tryptophan (1 g b.d.) and thioridazine (100 mg t.i.d.) but, despite four weeks on this regime, her mental state deteriorated and remained refractory to six further ECTs. Her hallucinations were prominent, she was sleeping only two or three hours a night, showed virtually no diurnal variation, and had become increasingly agitated. We decided to add flupenthixol to her regime, the depot form being chosen because of previous non-compliance: 20 mg was given initially and 40 mg three days later. Five days later she began to improve rapidly, with marked attenuation of hallucinations, sleep disturbance, and social withdrawal. Twenty-four hours later she was expressing optimism regarding the future, the first such emotion in over two years. Fortnightly injections were planned. Three days after her next injection she suddenly relapsed, but eight days later she improved. Two further cycles of eight days well and eight ill followed. We attempted to rationalise her medication by replacing thioridazine with flupenthixol, but, despite increasing flupenthixol, we were unable to reduce her thioridazine. Indeed, a pattern of decreased well-being on increased doses of flupenthixol developed, no symptomatic relief being obtained on 80 mg flupenthixol fortnightly.

At this stage further injections were withheld, in the expectation of clinical improvement. Nine days later (23 days after 80 mg flupenthixol had been administered) improvement began. The following day 20 mg was administered. Improvement continued until seven days later, when she claimed to be "as well as I have ever been". A regime of 20 mg fortnightly was adopted. On this regime, withdrawal of thioridazine and L-tryptophan and halving the dosage of clomipramine had no adverse effect on her mental state, and she remained free from affective symptomatology until her discharge six weeks later. Three weeks after discharge she began to deteriorate, hallucinations returning after a further three weeks and re-admission occurring one week later. She admitted not taking her clomipramine after discharge, although she had received flupenthixol injections as planned. Six days after reintroduction of clomipramine (150 mg/day) she began to improve.

Since the patient's medication regime was uncontrolled, it is not possible to draw firm conclusions about her response. However, improvement occurred only when flupenthixol and clomipramine were given in combination, and was maintained only with a dose of flupenthixol not normally considered antipsychotic. Indeed, beneficial effects were lost at higher doses. It is therefore unlikely that improvement was due to either agent alone. The close relationship between her mental state and manipulation of her medication make spontaneous fluctuation unlikely. Johnson & Malik (1975) describe mood elevation in the seven days following flupenthixol injection – our patient did not show this pattern.

It is likely that her response is unrelated to the antipsychotic effects of flupenthixol. It has been

assumed that the antidepressant effect of flupenthixol is manifested at lower doses than the anti-psychotic effect – although this has never been proven by case studies or clinical trials. The most likely explanation for her response is an interaction between clomipramine and flupenthixol, not involving the anti-psychotic effects of the latter, the rapidity of the response to the drugs in combination suggesting synergism between the two compounds.

Illness episodes of this chronicity and severity are uncommon and we think that the fact that she responded to the combination is encouraging. More case reports of such efficacy in resistant depression would be necessary to assess the feasibility of this regime being used in a clinical trial in this condition.

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Water Intoxication in Congenital Neurosyphilis

SIR: Water intoxication may occur in almost any psychiatric disorder (Ferrier, 1985), but this is the first report of it in congenital neurosyphilis. In about 80% of cases of water intoxication the patients are psychotic (usually schizophrenic). Although this patient was psychotic, mentally retarded, and had some abnormal neurological signs, the precise diagnosis of congenital neurosyphilis was delayed, as by the time she was seen VDRL and TPHA were negative and Hutchinson's teeth had been extracted.

Case report: A 48-year-old mentally retarded woman was admitted to a psychiatric ward after she violently attacked her 75-year-old mother, with whom she still shared a bed at night. Prior to admission she was doing little apart from smoking heavily (80 cigarettes a day) and drinking fluids excessively. Each day she would consume 3 pots of tea, 6 pints of milk, 2.5 litres of orange juice, and an unknown quantity of water directly from the taps. The patient had three previous admissions to the psychiatric unit. The first time, at the age of 45, diagnoses of mental retardation, alcoholism, and depression with obsessional and hypochondriacal features were made. The second admission (aged 46) followed her attempt to set fire to her home. She was still abusing alcohol (8–10 pints of beer per day) and was depressed. While in hospital she drank water to such an extent that she developed hyponatraemia, hypokalaemia, and had *grand mal* seizures. During the third admission (at the age of 47) she was still drinking alcohol and water excessively, and was thought to be depressed. Following discharge she did not abuse alcohol, but continued to drink water as before. On this fourth occasion she presented as a slim, dishevelled, perplexed woman who was incontinent of urine. She was agitated, incoherent at times, mumbled, and drew a cross on my forehead with her finger and prayed, but was unable to explain why. She was disorientated in time and place, described herself as being frightened and everything around her as being larger (macropsia). There were no auditory hallucinations or systematised delusions. Physical examination of cardiovascular and respiratory systems was normal. There was an abdominal scar from a duodenal ulcer operation. Central nervous system examination showed decreased visual acuity and two small aneurysms in the right eye. The right knee jerk was absent and the right plantar response was up; the left plantar response was normal. The ankle jerks were absent. Proprioception was impaired, but more on the right side. Pin prick showed glove and stocking peripheral neuropathy. She had a tremor of both hands. Her gait was slightly ataxic. Musculoskeletal system was normal apart from swelling over right knee and left ankle.

Investigations: FBC, thyroid, liver function tests, serum glucose, midstream urine culture, ECG, and EEG were normal. VDRL, TPHA, FTA were negative. CT scan showed minimal degree of general cerebral atrophy. Urea, calcium, sodium, and potassium were below the lower end of the reference range, in keeping with excessive water intake. Urinary osmolality was 116 mosmol/kg (reference range 40–1400) and plasma osmolality was 277 mosmol/kg (reference range 275–295). Old case notes were obtained from the Rheumatology Department; those stated that at the age of 19 (when she presented with backache) her Hutchinson's teeth were noticed. WR was found to be negative, TPI positive, and CSF gave a typical Lange curve. She was treated with a full course of penicillin and Hutchinson's teeth were extracted.

Progress: following administration of trifluoperazine (15 mg nocte, orally) her fluid intake decreased, she became continent, and her mental state improved, but the serum electrolytes were still abnormal, so demeclocycline (250 mg q.d.s.) was added. Further restrictions on water intake and cigarette smoking were made. On discharge her mental state was normal apart from mental retardation (IQ 63) and slight memory defect. Her fluid intake was 1.9 litres daily, and all electrolytes were normal. Two weeks later she stopped taking her medication and soon had a relapse. The same treatment was attempted on an out-patient basis, and she again improved.